

## **REMARKS**

### **Claim Amendments**

Claims 1, 3-12, 14-20, 22-23, 25-27 and 31-32 are pending. Claims 2, 13, 21, 24 and 28-30 have been previously cancelled. Claims 1, 10 and 31 are amended. Support for the amended claims may be found at page 7, line 6 to 10 of the specification. The amendments are being made solely to advance prosecution of this application to allowance and do not constitute an acquiescence, abandonment or disclaimer with respect to any subject matter originally claimed. Applicants reserve the right to pursue any excluded subject matter by way of one or more further application(s).

### **Specification Amendments**

The fifth linear depiction in Figure 2 utilizing a dotted line with small squares represents the background fluorescence. The description of Figure 2 at page 5 of the specification has been amended to specify this.

### **Claim Rejections – 35 U.S.C. §112**

The Examiner has rejected claims 1, 3-8, 10-12, 20, 22, 23 and 25-27 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse the rejection.

The Examiner considers that it is unclear whether a subject having normal levels of LL-37 is impervious to infection or has a decreased susceptibility to infection. Independent claims 1 and 10 have been amended to specify that no LL-37 or a lowered level of LL-37 “*indicates that said subject has an increased susceptibility to infection.*” This is in line with the teaching in the specification that a subject exhibiting no LL-37 or low levels of LL-37 compared to a control subject has an “*increased susceptibility*” to infection.

Independent claims 20, 23 and 25 do not state that no LL-37 or a lowered level of LL-37 “*indicates that said subject is susceptible to infection.*” Therefore, the Examiner’s arguments do not apply to these claims.

Reconsideration and withdrawal of the rejection made under the second paragraph of 35 U.S.C. §112 are respectfully requested because the amended claims are clear and definite.

The Examiner has rejected claims 9, 14-19, 31 and 32 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not reasonably provide enablement for compositions for or methods of treatment *in vivo*. Applicants respectfully traverse the rejection.

At the priority date, LL-37 had not been used to treat or prevent infection *in vivo*. However, it had been demonstrated in the art that LL-37 can successfully be delivered *in vivo* either by injection of the peptide or by delivery of a nucleic acid encoding LL-37 such that the LL-37 retains biological activities.

Koczulla *et al.*, *J. Clin. Invest.*, 111:1665-1672 (2003) (a copy of which is being cited and provided with the accompanying SIDS) demonstrates that LL-37 can be injected into muscle and that the injected LL-37 has biological activity as it is able to induce angiogenesis (see page 1666, right column, last paragraph and page 1667, paragraph spanning left and right columns). Therefore, tissue availability and *in vivo* activity of an administered LL-37 peptide have been demonstrated in the prior art.

Bals *et al.*, *Infection and Immunity*, 67:6084-6089 (1999) (previously cited as Reference No. AY4) describes the systemic expression of LL-37 after intravenous injection of recombinant adenovirus encoding LL-37 in mice such that the innate immune response was augmented (see abstract). Therefore, the ability of exogenous LL-37 to affect the immune response *in vivo* had also been demonstrated in the prior art.

Methods of administration and doses of LL-37 are given in the specification at page 19 line 30 to page 22 line 2. Furthermore, it had been demonstrated in the prior art that other peptides have anti-microbial activity and the prior art teaches how to determine an effective

amount of the anti-microbial peptide. For example, Mosca *et al.*, *Anti-Microbial Agents and Chemotherapy*, 44:1803-1808 (2000) (a copy of which is being cited and provided with the accompanying SIDS) describes the treatment of oral mucositis using the anti-microbial peptide IB-367. This document provides a demonstration that anti-microbial peptides administered to the oral cavity have anti-microbial activity and demonstrate that the concentration of peptide to be used depends on the minimum inhibitory concentration (MIC) of the peptide (see abstract). It would be entirely straightforward for the skilled person to determine the MICs for LL-37 using standard techniques (such as those described at page 1804, left column, third paragraph of Mosca *et al.*) and hence to determine the concentration at which LL-37 would be efficacious *in vivo*.

Thus, in summary, the *in vivo* activity of LL-37 and its bioavailability had been demonstrated in the prior art. It was also known in the art that anti-microbial peptides retain their anti-microbial properties following oral administration and so the skilled person reading the present specification would recognize that LL-37 could be administered in the same way. In addition, the present specification discloses suitable administration methods and doses of LL-37. Accordingly, the skilled person would be able to make LL-37 compositions and use them in methods of treatment.

Reconsideration and withdrawal of the rejection made under the first paragraph of 35 U.S.C §112 are requested because the specification enables a person skilled in the art to which it pertains, or in which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

#### **Information Disclosure Statement**

A Supplemental Information Disclosure Statement (SIDS) is being filed concurrently herewith. Entry of the SIDS is respectfully requested.

**CONCLUSION**

Having fully responded to all pending rejections contained in the Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicits an early notice to that effect. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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